

REMARKS

Appreciation is expressed to the examiner for the helpful interview. The following summarizes its substance.

Claims 33-34 have been canceled without prejudice or disclaimer of the subject matter recited therein. The amendment to claim 29 is supported, e.g., by page 35, lines 1-6, 27-31 and 36, and page 37, lines 20-22, as well as by the listing of compounds in claim 26, particularly at the bottom of page 100 and following. It is believed the examiner agreed to this amendment during the interview. Support for claim 44 is at the paragraph bridging page 37 and 38 and the examples, etc. Support for new claim 45 can be found in the structure of compounds 44 and 45 (pages 59 and 60 of the specification). This claim is identical to claim 29 except for the definition of L⁴. New claims 36-38 reinstate previously fully examined method claim 24. The specification changes make obvious changes additional to those previously made.

The allegation that Ohno et al. anticipates the claimed invention is unfounded. Ohno et al. discloses photosensitive materials containing a very broad class of dyes of formula I (see column 3 of the patent). This reference does not disclose the class of sodium salts instantly claimed. Nothing in Ohno et al. leads a skilled worker to the claimed subject matter.

The example cited by the Examiner (Example 13, column 7-8 of Ohno et al.) is a potassium salt. Ohno et al. discloses, in conjunction with its very broad class of molecules in column 3, a list of exemplary salts. Nothing in Ohno et al. would lead one, when viewing example 13, to select a salt variation of example 13 from among the very many modifications possible from column 3. On this basis alone, there is no anticipation. But even if one did choose to vary the salt using impermissible hindsight, nothing leads one to select the Na⁺ salts recited in the instant claims from among the many other salts disclosed, including even "organic" ammonium salts. In this regard, the Federal Circuit has held that a reference must clearly and unequivocally disclose the claimed compounds or direct those skilled in the art to make the particular selection necessary to arrive at the claimed subject matter. *In re Arkley*, 455 F.2d 586 (C.C.P.A. 1972).

Accordingly, applicants respectfully request withdrawal of this rejection.

It is believed agreed that Ohno et al. is the closest prior art. Turner et al. does not even generically suggest compounds with a substitution at L⁴. Neither does Lonsky et al. It is irrelevant whether Lonsky et al. teaches how to make sodium salts of cyanine dyes. What is relevant is whether Turner et al. and/or Lonsky et al. motivate a skilled worker to make compounds as claimed including the L⁴ structure. Even if Lonsky et al. had suggested L⁴, Turner et al. still would not lead one to the claimed structures from its very broad genus.

As discussed in the interview, neither Ohno et al. in general, nor its specific K⁺ compounds, render the claimed Na⁺ compounds obvious. There are so many structural variations possible from column 3 of Ohno et al. that nothing motivates a skilled worker to modify by only replacing K⁺ by Na⁺.

Supplementally, the specification contains data which establishes that the claimed Na⁺ compounds are unexpectedly advantageously less toxic (higher *in vivo* tolerability) than the corresponding K⁺ salts. See Table 5 on page 84. (Under *In re Soni*, 34 USPQ2d 1684 (Fed. Cir. 1995), it is unnecessary to submit these experiments in declaration format.) For convenience, the most pertinent of these data for the current claims are repeated in the attached Table, along with the structures involved.

The examiner apparently relies on example I-13 (column 8) of Ohno et al. as the closest prior art species. (See also column 6, compound I-5.) As the examiner notes, such compounds have 4 carbon atoms in the alkyl chain connected to the N-atoms of the molecules. These compounds also differ in degree of sulfonation. In the comparative data, compounds 31 and 43 have two or four, respectively, carbon atoms in the same position and also have different degrees of sulfonation. As the data show, the sodium salts of compounds 31 and 43, in each case, have unexpected and significant superiority in LD₅₀ values compared to the corresponding potassium salts. See page 84, last two lines, of the specification. Ohno et al. discloses only the potassium salts of its closest prior art compounds, not the sodium salts.

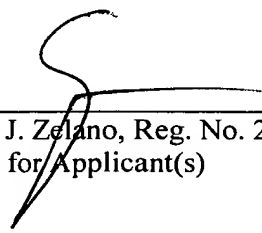
Thus, the data establish that the sodium salt compounds of this invention are unexpectedly superior over the closest prior art potassium compounds of Ohno et al. (Similar results are also shown for the sodium versus potassium salts of compound 45. For the sake of completeness, applicants also note that other properties (e.g., protein binding, partition coefficient, fluorescence quantum yield in plasmid or water) are not significantly different for the sodium and potassium salts, e.g., of compound 31. Under *In re Chupp*, 816 F.2d 643 (Fed. Cir. 1987), the claims are nevertheless still patentable.)

Based on all the foregoing, it is respectfully submitted that the claims of this application are allowable.

A copy of an office action in copending application 10/149,417 is being filed herewith.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



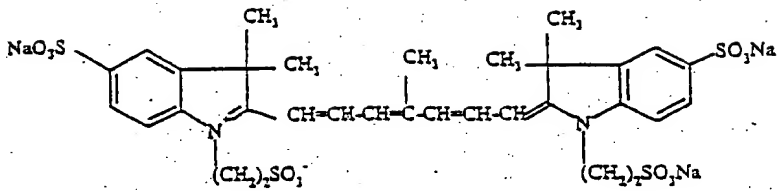
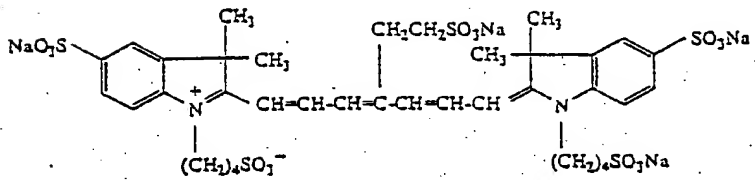
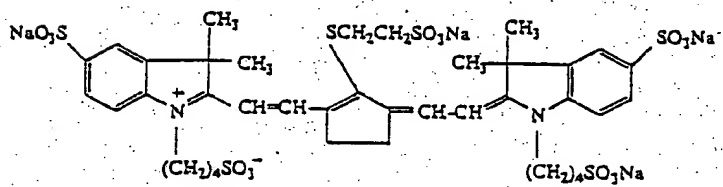
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Date: April 12, 2004

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TABLE

<u>Compound No</u> ²	<u>LD₅₀</u> ¹ (mg/kg)	
	<u>Na salt</u>	<u>K salt</u>
(31)		>3550
(43)		1630
(45)		1100-1220

¹ Na salt only shown; K salt identical in structure except for Na replacement

² LD₅₀ values are from Table 5 of specification (page 84), Experimental Example 5